

# Clinical features of adult and pediatric anaphylaxis in Taiwan

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## Summary

**Background:** Most epidemiologic studies of anaphylaxis have been on Western populations, leaving the clinical and demographic pattern of this acute allergic condition in Asia unclear.

**Objective:** To investigate the clinical characteristics of patients with anaphylaxis in Chang Gung Memorial Hospital, the largest medical center in Taiwan.

**Methods:** We conducted a retrospective analysis of 201 patients who visited the emergency department or were admitted to the hospital for anaphylaxis from 2000 to 2010. We analyzed the causes, clinical presentation, and management, and also compared adult and pediatric cases.

**Results:** The average patient age was 43.3 years. Mortality from anaphylaxis was 0.5% (1/201). The annual number of cases presenting with anaphylaxis increased throughout the decade we studied. Seven types of etiology were identified: medication (53%), contrast medium (24%), idiopathic condition (8%), food (5%), blood transfusion (4%), insect sting (3%), and others (3%). Skin and respiratory presentations are more common in children than in adults (skin presentation, 81% vs. 51%,  $p = 0.002$ ); respiratory presentation, 74% vs. 49%,  $p = 0.011$ ), and cardiovascular presentation is more frequent in adults than in children (83% vs. 61%,  $p = 0.006$ ). Clinical presentations with angioedema, gastro-intestinal and neurological system involvement, and management were not significantly different between adults and children.

**Conclusions:** We conclude that anaphylaxis in Taiwan appears to be increasing, just as in the West, but shows a different clinical picture; medication rather than food was the most common cause of anaphylaxis in our population. Moreover, food-induced anaphylaxis in children is not so prevalent in Taiwan. (*Asian Pac J Allergy Immunol* 2011;29:307-12)

**Key words:** anaphylaxis, epidemiology, etiology, Taiwan, Asia, Chinese

## Introduction

Anaphylaxis is a severe acute allergic reaction, which can involve multiple organs and even pose an immediate threat to life. Anaphylaxis is a true medical emergency, which calls for early recognition and prompt action. The prevalence of anaphylaxis, especially in the pediatric age group, has markedly increased during the past decades.<sup>1-5</sup> Many experts work towards a better understanding of anaphylaxis with the aim of preventing tragedy, but the rarity and irreproducibility of anaphylaxis render its investigation difficult. Most published studies about anaphylaxis have been carried out in Western countries such as the United States, the United Kingdom, and Australia. Thus, the characteristics of anaphylaxis in Asia and how these differ from those in the West are not clear. Similarly, little is known about the differences between children and adults with regard to this condition. For a better understanding of these factors as well as the overall clinical pattern of anaphylaxis in the Asian population, particularly the Han Chinese, we analyzed patients who presented to Chang Gung Memorial Hospital in the past decade.

## Methods

We identified all patients who presented to Chang Gung Memorial Hospital with anaphylaxis between January 1, 2000 and October 30, 2010. Patients discharged with a diagnosis of anaphylaxis either from the emergency department or from the wards were selected using the relevant International

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**Table 1.** Demographic characteristics of patients with anaphylaxis in Chang Gung Memorial Hospital from 2000 to 2010.

	Overall	Children	Adult
Patient number	201	31	170
Mean age (range)	43.3 years (3months-92years)	7.9 years (3months-18years)	52.2 years (19-92years)
Male: Female	106 : 95	15 : 16	91 : 79
Presentation outside hospital	43%	77%	37%
Atopy			
atopic dermatitis	5%	26% *	1%
allergic rhinitis	7%	16% *	5%
asthma	9%	32% *	5%
sensitization	17%	42% *	12%

\*Significant difference, defined as *P* value < 0.05

Classifications of Diseases-ninth revision (ICD-9) diagnostic codes. These codes included 995.60 (anaphylactic shock caused by unspecified food), 995.61–995.69 (anaphylactic shock caused by specified food), and 995.0 (other anaphylactic shock). Through a retrospective review of medical records, we collected the following data: patient age, sex, vital signs at presentation, suspected etiology of anaphylaxis, medical history, clinical presentation, treatment, course of hospitalization, outcome, and follow-up results. Patients who fulfilled the consensus definition of anaphylaxis were enrolled in this study group. We used the definition of anaphylaxis adopted from the second National Institute of Allergy and Infectious Disease (NIAID) and the Food Allergy and Anaphylaxis Network (FAAN) symposium (2005).<sup>6</sup>

The statistical software Stata 10.0 was used to analyze our data. Data are expressed as means and percentages (95% confidence interval [CI]). We had 2 subgroups in the data set, one consisting of children and the other of adults. The  $\chi^2$  test was performed to compare the 2 subgroups and to investigate their independence from the other. A two-tailed *P* value lower than 0.05 was considered to indicate a statistically significant difference.

## Results

Two hundred and one patients were admitted to the Chang Gung Memorial Hospital or visited its emergency department for anaphylaxis from 2000 to 2010 and had a discharge diagnosis of anaphylaxis. Our study group contained 95 female and 106 male patients (170 adults and 31 children). The average age was 43.3 years (adults, 52.2 years; children, 7.9 years). Anaphylaxis occurred outside of the hospital

**Table 2.** Etiology of anaphylaxis in Chang Gung Memorial Hospital from 2000 to 2010.

	Overall Number (%)	Number of pediatric cases (%)	Number of adult cases (%)
1.Food	10 (5%)	6 (19%) Shrimp 1 Egg 2 Other food 3	4 (2%) Shrimp 2 Wine 1 Other food 1
2.Medications	106 (53%)	13 (42%) NSAIDs 5 Antibiotics 1 Chemotherapy 1 AEDs 1 Biologics 1 Other drug 4	93 (54%) NSAIDs 18 Antibiotics 25 Chemotherapy 12 AEDs 2 Biologics 2 Other drug 34
3.Insect sting	6 (3%)	0 (0%)	6 (4%)
4.Idiopathic	15 (8%)	7 (23%)	8 (5%)
5.Constrast medium	49 (24%)	3 (10%)	46 (27%)
6.Blood transfusion	8 (4%)	0 (0%)	8 (5%)
7.Others	7 (3%)	2 (6%) Immunotherapy 2	5 (3%) Pesticides 1 Anesthesia 3 Swine flu H1N1 vaccine 1

NSAIDs: Non-steroidal anti-inflammatory drugs; AEDs: anti-epileptic drugs

in 43% of the cases (Table 1). The mortality rate was 0.5% (1/201).

In the past decade, the annual number of patients with anaphylaxis and the occurrence rate of anaphylaxis observed in Chang Gung Memorial Hospital has increased. Fourteen anaphylaxis events occurred in 2000 and 25 in 2010. The incidence of anaphylaxis elevated from 4.7 per 100,000 patients in 2002 to 12.8 per 100,000 patients in 2010. A peak, up to 14.5 per 100,000 patients, was noted in 2007 (Figure 1). Seven etiological categories were identified (Table 2), including medication (53%; 54% in adults, 42% in children), contrast medium (24%; 27% in adults, 10% in children), idiopathic condition (8%; 5% in adults, 23% in children), food (5%; 2% in adults, 19% in children), blood transfusion (4%; 5% in adults, 0% in children), insect sting (3%; 4% in adults, 0% in children), and others (3%; 3% in adults, 6% in children).

Of the 201 patients with episodes of anaphylaxis, 55% presented with skin-related symptoms such as urticaria and wheals, 20% presented with angioedema, 18% had gastrointestinal system involvement, 80% had cardiovascular symptoms and signs, 27% had neurologic manifestation and 53% had respiratory system-related symptoms. With regard to management, 57% received an epinephrine

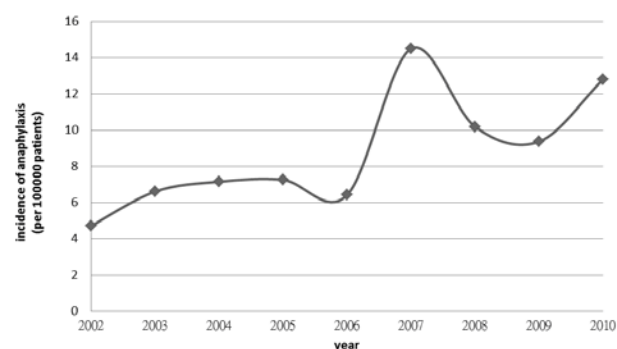
**Table 3.** Clinical features of patients with anaphylaxis in Chang Gung Memorial Hospital from 2000 to 2010.

	Overall (%) [95%CI]	Children (%) [95%CI]	Adult (%) [95%CI]	P value
<i>Clinical presentation</i>				
Skin	55 [48–62]	81 [63–93]	51 [43–58]	0.002 *
Angioedema	20 [15–26]	32 [17–51]	18 [12–24]	0.061
Cardiovascular	80 [73–85]	61 [42–78]	83 [76–88]	0.006 *
Gastrointestinal	18 [13–24]	29 [14–48]	16 [11–22]	0.079
Respiratory	53 [46–60]	74 [55–88]	49 [42–57]	0.011 *
Neurologic	27 [21–34]	29 [14–48]	27 [21–34]	0.821
<i>Management</i>				
H1 antagonist	77 [71–83]	81 [63–93]	76 [69–83]	0.600
H2 antagonist	5 [2–8]	3 [0–17]	5 [2–9]	0.710
Corticosteroid	81 [75–87]	77 [59–90]	82 [75–88]	0.535
Epinephrine	57 [49–63]	45 [27–64]	59 [51–66]	0.166
ET intubation	17 [12–23]	10 [2–26]	18 [13–25]	0.238
Fluid challenge	60 [52–66]	55 [36–73]	60 [53–68]	0.565
CPR	9 [5–13]	10 [2–26]	8 [5–14]	0.798
Inotrope use	29 [22–35]	19 [7–37]	30 [23–38]	0.220

ET: endotracheal; CPR: cardiopulmonary resuscitation.

\*Significant difference, defined as *P* value <0.05

injection, 81% received corticosteroid, 77% received an antihistamine H1 antagonist, and 5% an antihistamine H2 antagonist; 29% required an inotrope, 60% were given a fluid challenge, 17% required endotracheal intubation and mechanical ventilation, and 9% underwent cardiopulmonary resuscitation (Table 3). Each of the above parameters was compared between children and adults. Among the clinical manifestations, skin and respiratory system-related presentations were more common in children than in adults (skin manifestation, 81% vs. 51% ( $p=0.002$ ); presentation with respiratory symptoms, 74% vs. 49% ( $p=0.011$ )), while adults present more frequently with cardiovascular symptoms (83% vs. 61%,  $p=0.006$ ). The frequency of angioedema, and gastrointestinal and nervous system involvement at presentation was not significantly different between the 2 groups, nor was the line of management chosen. We found that manifestations of atopy, asthma, allergic rhinitis, atopic dermatitis, and sensitization were higher in children with anaphylaxis than in adults with anaphylaxis ( $p<0.05$ ) (Table 1).

**Figure 1.** The annual incidence of anaphylaxis in Chang Gung Memorial Hospital increased from 4.7 per 100,000 patients in 2002 to 12.8 per 100,000 patients in 2010. The peak was 14.5 per 100,000 patients in 2007.

## Discussion

This is the first epidemiologic report of anaphylaxis in Taiwan and could be one of the pioneer studies in Asian anaphylaxis. Most published research on anaphylaxis is based on data from Western countries and their results might not apply entirely to the Asian population as Asia is distinct from Western countries with regard to various aspects such as ethnicity, food, life style, and diseases. Therefore, we believe that the clinical and demographic pattern of anaphylaxis in Asia merited investigation. Our study is the first retrospective review of this condition in Taiwan, where the majority of the population is Han Chinese. Through our study, we found that the features of anaphylaxis are not identical in Western and Asian countries.

The incidence of anaphylaxis is increasing all over the world. Our 11-year experience with anaphylaxis in Chang Gung Memorial Hospital revealed a similar trend; not only the number of anaphylaxis events but also the incidence of anaphylaxis rose through the past decade (Figure 1). Although each published study had its own methodology and definition of anaphylaxis, most studies concurred on the fact that a rising incidence is evident. The Rochester Epidemiology Project, a population-based study, revealed that the annual incidence rate increased from 46.9 per 100,000 persons in 1990 to 58.9 per 100,000 persons in 2000 ( $p=0.03$ ).<sup>3</sup> The age-specific rates of anaphylaxis were highest in the age group 0–19 years, up to 70 per 100,000 person-years in Rochester Epidemiology Project.<sup>3</sup> In England, Sheikh used QRESEARCH, a

national healthcare database, to calculate the incidence of anaphylaxis and found that the age-sex-standardized incidence of anaphylaxis was 6.7 per 100,000 person-years in 2001 and increased by 19%, to 7.9 in 2005.<sup>7</sup> Recent hospital-based anaphylaxis epidemiologic studies in Bangkok, Thailand also agreed with this increasing trend<sup>8,9</sup>. A 4.8 fold increase in the incidence of anaphylaxis during 1992-2001 was observed in the King Chulalongkorn Memorial Hospital.<sup>8</sup> The annual occurrence rate of anaphylaxis in Siriraj Hospital increased from 9.16 per 100,000 inpatients in 1999 to 55.45 per 100,000 inpatients in 2004.<sup>9</sup> Although we cannot fully explain this phenomenon, it might be related to rapid expansion of allergic diseases in general. In addition, according to second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium, 2005,<sup>6</sup> hypotension or shock is not essential to diagnose anaphylaxis. This relative broadening of the definition of anaphylaxis has partially contributed to the observed increase in the recorded cases.

The current study contributes to the existing knowledge of anaphylactic conditions, especially because some of our findings contrast with those from the Western studies. One of the differences is that food is not the major cause of anaphylaxis in Taiwan; medication or drugs are the most common etiology in both the adult and pediatric groups. In Western countries, food products are reported as leading causes of anaphylaxis, particularly in the pediatric age group. Up to 85% of pediatric emergency department visits for anaphylaxis in Melbourne were food-induced<sup>10</sup>. Even though the epidemiologic studies about anaphylaxis in Asia are few, food-induced anaphylaxis in Asia seems less prevalent than in Western countries. Drugs and contrast media grew as major causes of anaphylaxis in Asia. Drugs accounts for 44%-53% of anaphylaxis in our result and two Thailand reports.<sup>8,9</sup> However, food remained the leading cause of anaphylaxis in another three Asian studies, in which drugs followed as the second most common cause<sup>11-13</sup>. Besides, food-induced anaphylaxis in Asia presents a different pattern. Peanut and tree nut are important food allergens in the United States and Western countries<sup>14,15</sup> but relatively uncommon in Asia. Seafood instead of peanut is the popular cause of food-induced anaphylaxis in Thailand.<sup>8,9,13</sup> In our study, shrimp accounted for one third of food-induced anaphylaxis. Another difference is that the

anaphylaxis-related mortality rate is lower in Taiwan than in the Western countries. The mortality rate was 0.5% (1 in 201 episodes of anaphylaxis) in our study. Reviewing the data from the Western countries, fatal anaphylaxis occurs in 0.65 to 2% of cases, and results in 1-3 deaths per million every year.<sup>16-17</sup> The only mortality in our study happened outside the hospital. A delay in epinephrine injection and cardiopulmonary resuscitation might increase the risk of mortality. Fifty seven percent of anaphylaxis events in our study occurred inside the hospital. In a hospital situation, the staff act immediately and the patient receives an epinephrine injection earlier. On the other hand, we cannot reliably exclude underestimation of mortality in our study as some patients with idiopathic out-of-hospital cardiac arrest may have been missed.

When we compared the pediatric group with the adult group, we found that presentation with skin-related symptoms is more common among children than adults. In our study, 81% children and 51% adults with anaphylaxis showed a skin manifestation. A high frequency of presentation with skin manifestations in children was also observed in Western countries. Susan D. Dibs and M. Douglas Baker reviewed pediatric patients admitted to the Children's Hospital of Philadelphia for treatment of anaphylaxis between January 1990 and December 1994 and found that 93% (53/55 episodes) had dermatologic manifestations.<sup>18</sup> In the Emergency Department at the Royal Children's Hospital, Melbourne, a retrospective review of anaphylaxis cases from 1998 to 2003 was conducted, revealing the urticaria incidence to be 72% (88/123 episodes).<sup>10</sup> Among our patients, 83% of the adults and 61% of the children had a cardiovascular system-related presentation. The frequency of cardiovascular signs and symptoms in our study is much higher than that in Western countries. In the United Kingdom, 10% patients of anaphylaxis had cardiovascular symptoms.<sup>19</sup> In the United States, 11% of anaphylaxis patients in Olmsted County suffered from hypotension.<sup>20</sup> In another US city, Rochester, Minnesota, 35.6% of patients had tachycardia and 12.6% had hypotension.<sup>3</sup> The higher percentage of cardiovascular presentation indicates that hypotension could be a major diagnostic clue indicative of this condition in Taiwan.

The post-anaphylactic follow-up protocol in our study was variable. Many patients from our study group were not subjected to a complete immunology

survey and did not receive an EpiPen prescription. Among our patients, 17% had sensitization, 12% were referred to the allergist, and only 1 patient had an EpiPen prescription. Because EpiPen was introduced in Taiwan in 2009 and is relatively expensive, this low rate of prescription is not unexpected. Contrast media and some medication induced anaphylaxis are classified as non-IgE-mediated anaphylaxis, so an allergist consultation and specific IgE blood test for allergen might be not arranged in such cases. This implies that more education about anaphylaxis is needed in Taiwan.

One limitation of our study is that we could not avoid underestimation. This was a retrospective study where patients were included on the basis of a matched ICD-9 code. We tried to find every possible case of anaphylaxis in our hospital, both in the Emergency Department (ED) and admissions unit. We assumed that every patient with anaphylaxis would either be referred to the ED or be recommended hospital admission for further evaluation. Thus, we may have missed a small group of mild non-fatal cases of anaphylaxis that presented to the outpatient department.

## Conclusion

The incidence of anaphylaxis in Taiwan is increasing, just as in the West, but shows a different clinical picture. According to our 11-year-experience in Taiwan, medication rather than food is the most common cause of anaphylaxis. Food-induced anaphylaxis is not highly prevalent in Taiwan.

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## Appendix. Summary of recent epidemiologic studies of anaphylaxis in Asia.

Hospital (reference)	Source	Duration, Location	Number of anaphylaxis cases	Occurrence rate of anaphylaxis	Causes		Clinical presentations (%) (by organ system)				
					Drugs	Contrast media	Foods	Skin	Res	CV	GI
King Chulalongkorn Memorial Hospital (5)	IPD	1992-2001 Bangkok, Thailand	79 cases	0.017%, 2.6 to 46 per 100,000 inpatients	48%	6%	31%	95	78.8	70	23.8
Siriraj Hospital (6)	IPD	1999-2004 Bangkok, Thailand	101 cases	9.16 to 55.45 per 100,000 admitted persons	44%	7%	24%	87	81	53	36
Seoul National University Hospital (7)	IPD OPD ED	2000-2006 Seoul, Korea	138 cases	0.014%	20.3%	14.5%	21%	95.7	74.6	76.8	34.8
Thammasat University Hospital (9)	ED	2003-2004 Patumthani, Thailand	64 cases	223 per 100,000 patients per year	36%	2%	40%	94	77	48	69
Bhumibol Adulyadej Hospital (10)	ED	2005-2006 Bangkok, Thailand	64 cases	52.5 per 100,000 patients per year	28.1%	---	56.3%	96.8	65.5	46.9	40.6
Chang Gung Memorial Hospital (our study)	IPD ED	2000-2010 Taoyuan, Taiwan	201 cases	4.7 to 14.8 per 100,000 patients	53%	24%	5%	55	53	80	18

ED: emergency department; IPD: inpatient department; OPD: outpatient department; Res: respiratory; CV: cardiovascular; GI: gastrointestinal